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# Syphilis — Current Status of Follow Up Study of The Treated Case

By Maurice R. Vinikoff, M. D., Director V.D. Division, El Paso City-County Health Unit

Some of the most frequent questions presented to the syphilologist are with regard to the follow up of treated cases of syphilis. Particularly the problem of persistent positive serologic reports, and the question of retreatment are raised.

One of the basic fundamentals to remember is to "treat the patient and not a laboratory report." The serologic studies are of inestimable value in the follow up program, but the clinical status of the patient is equally important.

### Adequate Therapy

Following adequate therapy, as previously described, one should expect clinical improvement and a regression of lesions in the early stages of syphilis, and either improvement or cessation of progression in late symptomatic syphilis. For example, in early syphilis, the chancre, lymphadenitis, condylomata, skin syphilides, etc., should heal within a period of one or two weeks. In late symptomatic syphilis certain lesions will heal such as tertiary skin syphilides, gummata, etc. Generally speaking, the early lesions will heal without any permanent damage but most of the late lesions will leave irreparable damage. Examples of irreparable damage include coronary ostial stenosis, aneurysm of the aorta, aortic insufficiency, optic neuritis with atrophy, transverse myelitis, etc. In these cases, if one can halt the progression of the disease, that is all that may be expected.

If the early lesions fail to heal, or the late lesions are not arrested, or if clinical recurrence or relapse occurs, retreatment or continuation of treatment is indicated. Once satisfactory clinical response is noted, periodic serologic examination should be performed. At our clinic serologic examination is made every three months for the first year or two following therapy, and then every six months for an indefinite period.

In primary, darkfield positive syphilis, the serologic report may be non-reactive. Some of these patients may never become reactive but a certain percentage will become reactive, because the immunological reagin response takes several weeks to develop. In these cases, a decline in the serologic titre should be progressive and become non-reactive within one year. If serologic reactivity persists beyond this period, retreatment usually with a larger dosage than the original therapy is indicated. The same applies to secondary syphilis with the exception that practically all cases of secondary syphilis have reactive serologic reports at the onset.

### Latent Syphilis

In latent syphilis, the serologic titre should fall to low levels or become non-reactive entirely. The earlier the case is treated, the greater is the possi-

*Dr. Vinikoff this month is substituting for Dr. Jack A. Bernard, regular conductor of this section.

CURRENT THERAPY

bility that the serologic study will become non-reactive. In treated syphilis of less than two years duration (early latent syphilis), with adequate therapy the percentage of non-reactive results should be fairly high in a one to two year period following therapy. This percentage may reach approximately eighty percent. Syphilis treated after more than two years duration will yield a greater number of so called sero-resistant cases and this is proportionate to the length of time that treatment has been delayed. Roughly speaking, if treatment has not been instituted for four or more years following infection, about forty to fifty percent of the cases will remain reactive to the standard serologic tests but will usually run a low titre. When reference is made to serologic tests in this article, it indicates the standard reagin tests such as the V.D.R.L., Kahn, Eagle, Kolmer, etc., and not the newer treponemal tests such as the T.P.I. (Treponema Pallidum immobilization test) and the R.P.C.F. (Reiter Protein Complement Fixation test), etc.

If one is to follow treated syphilitic patients serologically, the quantitative titre is imperative. A purely qualitative report is of no value except when it becomes non-reactive. Quantitative titres are expressed in terms of dilutions. The number of times that a serum can be diluted and still give a positive result is referred to as "dils" and is reported as "reactive—two, four, eight, 16 dils" etc., depending upon the reactivity of the serum. With some tests such as the Kahn, the titre is expressed in "units" and is based upon the number of "dils" multiplied by four. These are reported as "reactive—four, eight, 16, 32 units," etc. It makes no difference which type of test is performed, but in the follow up, the comparison of titres to determine the trend of reactivity should be made with the same type of test. A comparison of quantitative titres using different tests is not valid.

Too often, patients are retreated because of a persistent positive qualitative serologic test for syphilis when actually there is no basis for it. There is no specific titre above which treatment is indicated and below which the patient should be left alone. The most important factor in the serologic titre is its trend. Following therapy, there should be a significant and continued downward trend of the serologic titre. Should non-reactivity occur, this is an excellent result, but if there is a continued decline in the titre, good progress is indicated. Most patients who do not reach a non-reactive status usually reach a low titre and continue at this low titre level for long periods of time and may do so indefinitely (sero-resistant). If on the other hand there is no significant decline, or even an increase in titre over a reasonable period of time, then retreatment is indicated. It should be borne in mind that a rise in titre on one follow up serologic report of, let us say, from 16 to 32 "units" or "dils" is not as great a rise as the numbers might indicate. The 16 unit difference represents merely one dilution and may be interpreted by one observer as 16 and another as 32.

It is advisable in all cases to recheck the spinal fluid examination about one or two years following the original therapy in order to determine early involvement of the central nervous system. In patients with previously positive cerebro spinal fluids who have received adequate therapy, the cerebro spinal fluid usually shows rapid improvement. The cell count and protein determination fall rapidly to normal levels. The Colloidal Gold and Kolmer (or other reagin tests) usually decline in positivity fairly rapidly but require a longer period to reach low titres or non-reactivity (approximately one year). Here again, should satisfactory response fail to occur retreatment is indicated.

Pregnancy in the syphilitic woman has raised many questions in therapy. For the sake of brevity, only the procedures followed at the El Paso City-County Health Unit Venereal Disease Clinic will be given. In previously treated pregnant women, serologic examinations are made at least twice and preferably three times during pregnancy; one as soon as pregnancy is diagnosed, the others in the second and third trimester. Patients yielding non-reactive serologic reports are not treated, whereas those showing reactivity are retreated according to the schedule given in the second article of this series.

Any syphilitic mother who has a late abortion, gives birth to a stillborn fetus, or to a congenital syphilitic child, is retreated.

With regard to the serologic examination of the newborn, it is the practice at our clinic never to perform it prior to the third month. To do so only adds confusion to the problem. If the newborn appears normal, the blood is taken at three months and then again at one year. The reasons for the above are concerned with the immunilogic

responses of the mother and child. In early infancy, the child may carry over reagin from the mother's blood and give a reactive result when actually the child is not infected. Conversely, if the child becomes infected during late pregnancy there may not have been time for reagin to develop in the child and a non-reactive report might result. By waiting three months the reagin carried over from the mother will have cleared from the child's blood, and should the child be recently infected, there would have been adequate time for reagin to develop in the child. If the child shows clinical evidence of syphilis then the darkfield examination is the method of choice for diagnosis. X-Ray of the long bones, clinical examination, etc., are all useful.

Finally, a great deal of emphasis must be placed on the public health aspects of syphilis. Every contact, either sexual or familial, should be examined clinically as well as serologically. All sex contacts and marital partners of early infectious syphilis cases should be examined particularly for signs of early syphilis. In cases of latent or congenital syphilis, parents or siblings of the patient should be appropriately examined.

## Quarterly Cumulative Index Medicus To Be Discontinued

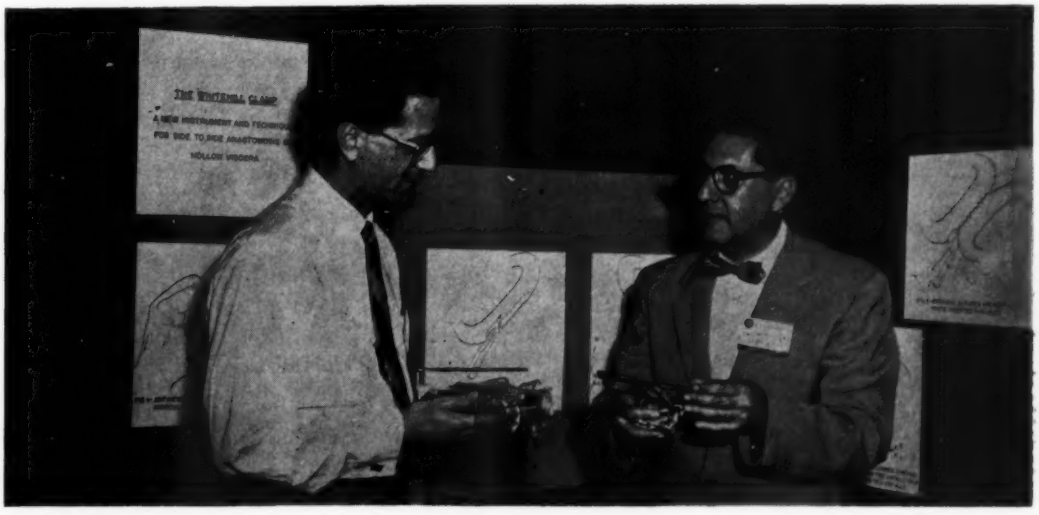
Word has just been received that the Quarterly Cumulative Index Medicus of the AMA will not be published in the future. Volume 65 will not be published.

This leaves the Current List of Medical Literature published through the National Library of Medicine by the U. S. Department of Health, Education and Welfare, Public Health Service at Washington, D. C. as the remaining publication of this type.

It has always been a source of pride to have a complete set of the Quarterly Cumulative Index Medicus. This publication has served a vital purpose in surveying and listing medical literature of the world. Through this publication a complete check could be made of previous published information and this was most helpful. This publication helped prevent the reduplication in medical publications.

It is the impression of this writer that the Current List of Medical Literature does not contain all of the publications in the world. It is hoped that this scope can be enlarged.

*AT AMA MEETING — Dr. J. L. Whitehill, Tucson, (right) holds a clamp which he devised for the anastomosis of hollow viscera as featured in the scientific exhibit at the recent AMA meeting in Atlantic City. Use of the instrument along with the technique which Dr. Whitehill suggests is said to reduce suturing time considerably. On the left is Dr. John A. Wilson, also of Tucson, who is holding a transparent plastic replica of the bowel showing how the wound looks after closure with this clamp.*



W. Compere Basom, M.D., *El Paso, Orthopaedic Editor*

# Importance of Instruments in Surgery

*(Continued from July Issue)*

It is a good idea to have a bone saw in a set. This is useful in amputations and shaping of bone grafts. Screw retrievers are also useful. The type made by Zimmer, Richards and DePuy are all in my set.

A brace with standard carpenter chuck with a full set of drill points and also long electrician drill points for certain intramedullary rod procedures are useful items.

A hack saw is useful in cutting pins and intramedullary nails.

I have a special operating room sterilizable box made by Wright Manufacturing Company of Memphis. This has small compartments, each one of which will contain a dozen stainless steel fine thread, single slot, self-tapping bone screws from one-fourth inch in length up to two inches.

### Hip Nailing Set

The hip nailing set also has space for the following:

Full set of Smith-Petersen Nails, stainless steel, serrated heads, cannulated center, requiring a 3/32nd inch diamond tip 9-inch stainless steel nail. The lengths of these nails are from 3 inches to 6 inches.

A full set of trochanteric anchor plates.

Several plain bolts for the attachment of the plate to the nail.

T-wrench.

Stainless steel guide pins, at least three with trocar points, plain hilt, each 9 inches in length for the guide pins.

Smith-Petersen nail driver.

Adapter for Jewett Nail.

Smith-Petersen nail starter.

Depth gauge.

Wire.

Special impactor.

Full set of drill points, large for the Smith-Petersen nails, small ones for the screws, 7/64ths of an inch in diameter.

In addition we have special sets of instruments such as the intramedullary rod set. This is in a large stainless steel box which can be autoclaved. It has two trays and it contains the extra-large diameter 11 x 13 millimeters, the medium size are 9 x 11 millimeters and also a smaller diameter rod and broaches for each nail. We use the Hansen-Street nail. We also have a modified set with threaded holes in the distal end suitable for fixation of the supracondylar fractures of the femur.

### Other Special Sets

The other special sets are hip prosthesis; we use the Fred-Thompson with vitallium and special instruments for it. A spine fusion set which contains special ronguers, reamers, lamina spreaders, bone mill and other curettes, rasps, spoon and retractors for spine fusion procedures, is employed.

A hand set, which includes special instruments for doing hand surgery, small drills for bone work, and instruments for tendon procedures, is used.

The external pin fixation set produced by the Tower people also is useful in certain procedures, particularly extremely comminuted fractures of the lower end of the femur, arthrodesis of the knee, certain fractures of the femur and tibia and forearm.

A Stryker bone saw with whole saw set and burrs has been useful.

The bone bank while not exactly an instrument, can be extremely useful in orthopaedic surgery procedures. It is very easy to prepare a peg graft for the use of hip fractures and for many other procedures if this is available.

In other words it is very helpful in orthopaedic procedures to have a full set of instruments available at the time of the operative procedure.

# MEETINGS

## Western Association of Railway Surgeons

*Dr. Winston*

**Cosmopolitan Hotel, Denver**

## Complete Program

**Thursday — September 10, 1959**

**9:00 a.m.** The Unique Responsibilities of a Railway Surgeon
John R. Winston, M. D.
Medical Director, A. T. & S. F. Ry. Company
President, Western Association of Railway Surgeons
Chicago, Illinois

**9:30 a.m.** Hypnosis And Its Use in Controlling Patients With Malignancy
Oscar L. Morphis, M. D.
Consultant in Radiology
A. T. & S. F. Railway Company
Fort Worth, Texas

**10:00 a.m.** Radioactive Isotopes and Medicine
Otto L. Hanson, M. D.
Chief of Medical Services
A. T. & S. F. Railway Company
Topeka, Kansas

**10:30 a.m.** INTERMISSION

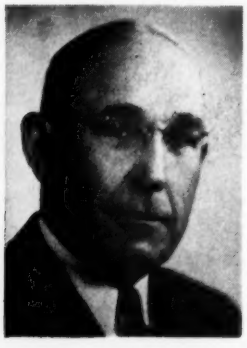
**11:00 a.m.** THE ANNUAL DOCTOR WILLIAM T. CUMMINS MEMORIAL LECTURE
Proposed Medical Standards for the Operators of Public and Commercial Vehicles
Seward E. Miller, M. D.
Director, Institute of Industrial Health
University of Michigan
Ann Arbor, Michigan

**Friday — September 11, 1959**

**9:00 a.m.** The Management of Trauma in Relation to Preventing Permanent Disability
Earl D. McBride, M. D.
Clinical Professor of Surgery
University of Oklahoma School of Medicine
Oklahoma City, Oklahoma

*Dr. Bargen*

*Dr. Brindley*



*Dr. Broders*

*Dr. Collett*

**9:30 a.m.** Recent Developments in the Management of Diabetes
E. Paul Sheridan, M. D.
Secretary, American Diabetes Association
Denver, Colorado

**10:00 a.m.** Clinical Neurological Problems Among Railway Operating Employees
D. Bernard Foster, M. D.
Neurologist, The Menninger Foundation
Topeka, Kansas

**10:30 a.m.** INTERMISSION

**11:00 a.m.** Symposium: Diseases of the Upper Gastro-Intestinal System
J. A. Bargen, M. D.
Chief of Medical Sections, Mayo Clinic
Rochester, Minnesota

G. V. Brindley, M. D.
Board of Regents, American College of Surgeons
Chief Surgeon, G. C. and S. F. Railway Co.
Temple, Texas

A. C. Broders, M. D.
Chief of Section on Pathology
Scott and White Clinic
Temple, Texas

N. C. Hightower, M. D., Director
Editorial Board
American Journal of Digestive Diseases
Temple, Texas

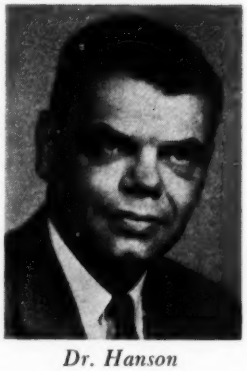
**Saturday — September 12, 1959**

**9:00 a.m.** Analysis of Two Thousand Herniorrhaphies
Waldo Newberg, M. D.
Chief of Surgical Services
Southern Pacific Hospital
San Francisco, California

**9:30 a.m.** Clinical Aspects of Long-Term Usage of Diuretics In the Management of Heart Disease
Benjamin S. Wells, M. D.
Director of Medical Education
Veterans Administration
Washington, D. C.

*Dr. Drisko*

*Dr. Foster*



*Dr. Hanson*

*Dr. Hightower*

*Dr. Hood*

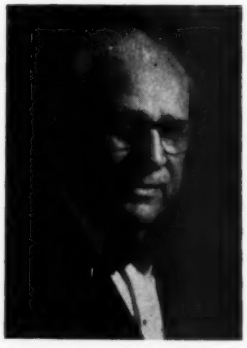
*Dr. Newberg*

**10:00 a.m.** Early Return to Duty Following Laminectomy For Herniated Disc

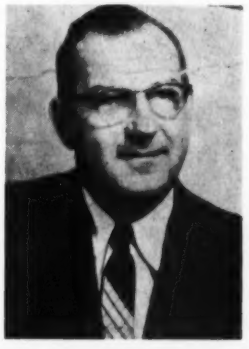
Robert M. Drisko, M. D.
Consulting Orthopedic Surgeon
Union Pacific and Kansas City Terminal Railroads
Kansas City, Missouri

Graham Owens, M. D.
Chief Surgeon, Kansas City Terminal Railway Company
Secretary, Western Association of Railway Surgeons
Kansas City, Missouri

*Dr. McBride*



*Dr. Owens*



**10:30 a.m.** INTERMISSION

**11:00 a.m.** Symposium: Diseases of the Colon

Dr. Hightower, Moderator
Dr. Bargen
Dr. Brindley
Dr. Broders

*Dr. Miller*

*Dr. Sheridan*

**12:00 Noon** The Diagnosis and Treatment of Temporal Mandibular Injuries

Hugh S. Collett, M. D.
Medical Department, Western Pacific Railway Company
Elko, Nevada

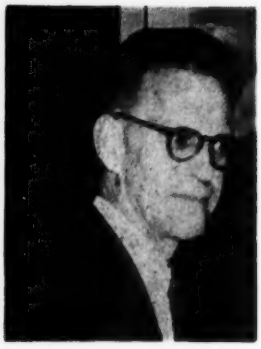
Thomas K. Hood, M. D.
Medical Department, Western Pacific Railway Company
Elko, Nevada

*Dr. Morphis*

*Dr. Wells*

Thursday and Friday noon there will be special activities for the Ladies, followed each afternoon by the Members and their Ladies visiting points of particular interest in the Denver area.

Friday evening the Ladies are invited to attend the Annual Banquet for which special entertainment is being arranged. The Ladies are also invited to meet with the members for Luncheon on Saturday noon.



*Dr. Babey*

*Edited By* ANDREW M. BABEY, M.D., LAS CRUCES, N.M.

## APHORISMS and MEMORABILIA

# Miscellaneous Truths and Concepts

*(Continued)*

**21.** ". . . a curious translucent appearance of the outer half of the soft part of the upper eyelid. If you look for this sign I am sure it will help you to spot cases which will improve on thyroid extract long before they develop into full-fledged myxedema."—HERBERT FRENCH, *Clin. J.*, 47-48: 135, 1918-19.

**22.** "We may have about any type and any degree of psychosis, chronic insanity or acute delirium in hyperthyroidism."—R. CABOT, *Case Record 6511*, Dec. 21, 1920.

**23.** "It may be remarked that in certain gouty patients the attacks of articular pain cease or diminish in severity when renal colic appears."—G. DIEULAFOY, *Textbook of Medicine*, D. Appleton & Co., 1912, p. 1886.

**24.** "Jaundice is one of the rarest complications of enteric fever."—C. ALLBUT, *System of icine*, Vol. 4, 1897, p. 99.

**25.** "Always remember salicylate delirium. We may get a very active psychosis, a maniacal state, from an overdose of salicylates. It may simulate psychosis, meningitis etc.—R. CABOT, *Case Record 6082*, Feb. 24, 1920.

**26.** "If a male patient with supposed strangulated hernia complains of pain running down the inner aspect of the thigh, it is well to think of torsion of the testicle."—BRICKNER AND MOSCHCOWITZ, *loc. cit.*

**27.** "Clubbing is one of those phenomena with which all physicians are so familiar that they appear to know more about it than they really do."—S. WEST, *Trans. Clin. Soc.*, 30:60, 1897.

**28.** "It is not generally known that temporary deafness sometimes results from excessive smoking, in smoking certain kinds of tobacco."—BYRON BRAMWELL, *Clinical Studies*, R. & R. Clark, Edinburg, vol 4, 1906.

**29.** "Never believe what a patient tells you his doctor has said." *Med. Axioms, Aphorisms and Clin. Memoranda*, J. A. Lindsay-H. K. LEWIS & Co., London, 1923, p. 5.

**30.** "Metastases to the spleen are common in sarcoma, uncommon in carcinoma."—TRACY MALLORY, *New England J. Med.*, 218: 1014, 1938.

**31.** ". . . in the aged there is a want of correlation between the local lesion and the production of general symptoms . . . the organism remains, so to speak, unmoved in presence of the gravest changes. The physician must redouble his attention and take into account the slightest indications, if he does not want to be surprised by completely unforeseen accidents."—C. M. CHARCOT, *Clin. Lectures on Chronic Diseases*, London, New Sydenham Soc., 1881, p. 38.

**Salient Danger**

**32.** "It is unnecessary—perhaps dangerous—in medicine to be too clever."—ROBERT HHTCHISON in address "Seven Gifts" before London Hosp. Med. College, *Lancet*, July 9, 1938, p. 61.

# ORIGINAL ARTICLES

## Apnea Associated With the Intraperitoneal Use of Neomycin

*By* C. Herbert Fredell, M.D.* and Bruce L. McElroy, R.N., *Flagstaff, Ariz.*

In recent years the treatment of peritonitis has improved greatly with the use of antibiotics by the combined parenteral and intraperitoneal administration. The intraperitoneal instillation of neomycin has been of definite value in lowering the mortality rate due to peritonitis.[4]

Gradually, as experience has accumulated, reports of apnea associated with the intraperitoneal use of neomycin have been published.[2] Experimental work has been done to elucidate the etiology of this phenomenon.[1,5]

The action of neomycin seems to be a potentiation or a combination with the anesthetic agent producing a neuromuscular blocking effect. The presence of peritoneal damage allows more rapid absorption of the neomycin consequently lowering the amount which might produce apnea.[1] Experimental and clinical work has shown that the apnea can be treated effectively with neostigmine methysulfate.[2]

Two cases are presented demonstrating this unusual problem.

**Case 1:**

An 86-year-old man was admitted to the Flagstaff Hospital on Dec. 7, 1957, complaining of cramping abdominal pain, nausea, vomiting, and obstipation of three days duration.

Physical examination revealed auricullar fibrillation and a distended tympanitic abdomen with diffuse abdominal tenderness. There were high pitched peristaltic sounds.

Under nitrous oxide, oxygen, pentothal, and anectine anesthesia an exploratory laparotomy was performed. There was an intestinal obstruction due to a perforated gangrenous appendix with severe generalized peritonitis. An appendectomy and lysis of adhesions was done. Prior to closure of the abdomen, five grams of neomycin sulfate dissolved in 500 cc's normal saline was used to lavage the peritoneal cavity. Within five minutes the patient was noted to be apneic. Edraphonium chloride (Tensilon) (35 mg) was given intravenously with no immediate effect.

During the next three hours the patient's ventalation was maintained by the anesthetist. The patient was then transferred into an Emerson respirator. One hour later the patient was breathing voluntarily and was fully conscious.

Post operative the patient was febrile due to his generalized peritonitis. He was disoriented on occasion due to mild azotemia which improved with hydration. He was discharged on the 10th post operative day.

Five months later he was readmitted to the hospital with cardiac failure and pernicous anemia expiring five days after admission.

**Comment**

This case demonstrates the use of neomycin intraperitoneally in the presence of severe intraperitoneal infection. The apnea that followed can best be accounted for on the basis of the instillation of a large dose of neomycin. The value of Tensilon in this case can not be evaluated. The spontaneous return of normal respiration can best be explained on the basis of detoxification during the period that the patient's respirations were maintained artificially.

**Case 2:**

This 111-year-old Navajo Indian male was admitted on July 22, 1958, complaining of nausea, vomiting, and cramping abdominal pain for an undetermined period of time. Language barrier prevented an adequate history.

*Chief of Surgery, Flagstaff Community Hospital, Flagstaff, Arizona

Physical examination revealed a tender, distended and tympanic abdomen. No peristaltic sounds were heard. Roentgen film of the abdomen revealed marked dilatation of the small intestine and the colon to the mid-transverse portion where it terminated abruptly.

Under nitrous oxide, oxygen, pentothal, and anectine anesthesia an exploratory laparotomy was performed. There was a perforated gastric ulcer one and one-half inches in diameter on the posterior aspect of the stomach which had drained into the lesser peritoneal sac. There was a large accumulation of fluid which had caused acute angulation of the transverse colon with obstruction. The perforation was plicated and the peritoneal cavity was aspirated.

Prior to closure of the peritoneal cavity, five grams of neomycin sulfate in 500 cc's of normal saline solution was used to lavage the peritoneal cavity. Within a few minutes the patient was noted to be apneic.

The patient was given 10 mg of edraphonium chloride (Tensilon) intravenously with no effect. The neomycin solution was aspirated from the peritoneal cavity. The patient was placed in the Emerson respirator. Three hours later his respiratory excursions were normal and he was fully conscious.

Postoperatively the patient had hypotension requiring constant intravenous vasopressor drug to maintain an adequate blood pressure and urinary flow. He had an incomplete heart block. His peritonitis improved but his cardiovascular status remained unchanged for the following eight days. At that time he had a complete heart block and went into congestive heart failure and expired.

**Comment**

This case demonstrates the effect of a large dose of neomycin instilled in the peritoneal cavity in the presence of peritoneal damage. In spite of immediate aspiration of a large amount of the solution, the patient became apneic. The Tensilon did not seem to be of any value. A period of three hours was required to maintain his respirations artificially before detoxification was complete.

**Discussion**

In view of our experience with these two cases, we believe the best management of this problem to be as follows.

Should neomycin be definitely indicated during the period of anesthesia in the presence of peritoneal damage the doseage should be small. (Not over one gram.)

The best method of administration of neomycin intraperitoneally is the placing of catheters in the appropriate locations in the peritoneal cavity at the time of surgery. When the patient has reacted from the effects of the anesthesia, then the neomycin can be instilled in a larger more effective doseage with much greater safety.

Should apnea occur following the intraperitoneal instillation of neomycin, immediate intravenous neostigmine methylsulfate (100-500 mgm) and maintaining respirations artificially is the best method of treatment. It may be necessary to maintain respirations for several hours before the effects of the drugs are overcome.

**Summary**


1. The dangers of the use of neomycin instilled intraperitoneally during a general anesthetic in the presence of peritoneal damage far outweigh any benefits accrued by this practice.
2. Two cases of apnea which occurred during these circumstances have been presented. Recovery in both cases has been noted.
3. Specific recommendations have been made concerning the use of neomycin in cases of peritoneal infection or injury.


**BIBLIOGRAPHY**


1. Gleidman, M. L., et al. Respiratory Arrest Following Intraperitoneal Administration of Neomycin, An Experimental Study, Surgical Forum, American College of Surgeons, Oct., 1958.
2. Middleton, W. H., Morgan, D. D., and Moyer, J., Neostigmine Therapy for Apnea occuring after administration of Neomycin. J.A.M.A. 165:218b, 1957.
3. Pittinger, C. B. and Long, J. P., Neuromuscular blocking action of neomycin sulfate, Antibiotics and Chemotherapy, 8:198-203, 1958.
4. Schatten, W. E., Interaperitoneal Antibiotic Administration in the Treatment of Acute Bacterial Peritonitis, Surg. Gynec. and Obst., 102:339-346. 1956.
5. Short, W. B., Hartley, J. L., Martin, J. D., A Study on Respiratory Arrest Following the Administration of Neomycin, Surgical Forum, American College of Surgeons, Oct., 1958.

# A New and Safe Enterokinetic Agent

By Eduardo Pena, M. D.* and Jose Padilla, M. D.**, *Miami, Fla.*

Gastrointestinal distress is a frequent complication following most major surgical procedures. This post surgical complication may assume degrees of severity ranging from a painful abdomen to an adynamic ileus with the result that vomiting and circulatory collapse may ensue.

Although the direct cause of post surgical intestinal atony is not fully understood, tissue traumatization, exposure, infection and manipulation of the intestines are all contributing factors. It now appears that chemical factors may also play a significant role. This concept has a sound biochemical basis, and its practical application has led to a new and promising approach to the management of postoperative adynamic ileus with pantothenic acid either as the salt or, preferably, its alcohol.

## Biochemical Function

Lipmann,[1] in 1945, elucidated the biochemical function of pantothenic acid, its participation in metabolic processes and, particularly, its relation to coenzyme A. The following diagram is based on Lipmann's research.

*Pantothenyl alcohol* converted by living organism to → Pantothenic acid

*Pantothenic acid* incorporated into → Coenzyme A

*Coenzyme A* in conjunction with Choline acetylase synthesizes Choline plus Acetate to Acetycholine

*Acetylcholine* acts on smooth muscle of G. I. tract, causing increased tone and peristalsis.

Lipmann's findings may explain the decrease in gastrointestinal motility observed in dogs[2] and rats[3] on diets deficient in pantothenic acid, and the correction of hypomotility through addition of pantothenic acid in the diet.

It was further demonstrated in rats and ducks maintained in a pantothenic acid deficiency state, that there was a 25 to 40 per cent decrease in coenzyme A content in all tissues.[4]

## Observations Applied

Applying these observations to the surgical patient, Stone et al.[5] suggest that surgical stress, circulatory disturbances and infection may cause a state of pantothenic acid deficiency which in turn would reduce formation of acetylcholine and thus predispose the post surgical patient to adynamic ileus. The numerous favorable reports of successful management of postoperative intestinal atony with pantothenic acid preparations tend to support the validity of the chemical concept.[5-12]

Since the results obtained with the usually employed methods (early ambulation, enemas, colon tubes, intubation, cholinergic drugs, pituitrin, etc.) have been equivocal, we were anxious to give d-pantothenyl alcohol* a trial in our surgical patients to determine if routine prophylactic administration would reduce or prevent the incidence of postoperative adynamic ileus.

## Study Group

The study group consisted of 45 patients on whom were performed various gynecological, obstetrical and gastrointestinal surgical procedures. The group was comprised of 39 females and 6 males ranging in age from 17 to 61 years. All operations were performed at either Mercy or Jackson Memorial Hospials, Miami, Florida. The kinds of procedures are presented in Table I.

**Table I**

| Operation | Number of Cases |
|---|---|
| Panhysterectomies | 19 |
| Hysterectomies | 3 |
| Bilateral salpingo-oophorectomies | 2 |
| Laparotomies | 3 |
| Anterior and posterior vaginal vault repair | 1 |
| Lysis of vaginal stricture | 1 |
| Caesarean section | 6 |
| Appendectomies | 3 |
| Hernia repair | 6 |
| Incision of perianal abscess | 1 |
| Total | 45 |

We administered intramuscularly two milliliters (500 mg. d-pantothenyl alcohol) immediately after surgery. Frequency of administration, thereafter, was at intervals of every six hours. Dosage was continued until bowel sounds returned in all

* Jackson Memorial Hospital, Miami, Florida
** Mercy Hospital, Miami, Florida
* Cozyme, Travenol Laboratories, Inc., Morton Grove, Ill.

four quadrants with the spontaneous evacuation of feces.

### Results

Thirty-five of the patients had a spontaneous bowel movement within 40 to 72 hours and eight had an evacuation within 24 hours after the initial dose of d-pantothenyl alcohol. Two patients did not respond. One, a 42 year old primipara with a breech presentation and a uterine inertia on the third day postoperatively, developed a paralytic ileus, and in spite of continued medication the ileus persisted. Normal peristalsis was restored in this patient by means of a Cantor tube. In the other individual, a 17 year old obese female, there was a slight evidence of bowel distention after four days' therapy.

### Discussion

It has been our experience that operations of the type reported usually predispose to the development of postoperative intestinal atony in varying degrees of intensity, and a prevention rate of 95 per cent is highly encouraging. We have continued to have success with d-pantothenyl alcohol in numerous similar surgical procedures not included in this report. We advocate the routine use of d-pantothenyl alcohol to be intramuscularly administered following surgical procedures as an effective preventive medication for postoperative ileus.

### Summary and Conclusions

**1.** In 45 patients who had undergone various gynecological, obstetrical and other intra-abdominal operations, no instance of postoperative paralytic ileus occurred in 43 after the intramuscular administration of d-pantothenyl alcohol started immediately after surgery.

**2.** Ordinarily such operative procedures introduce the liability of postoperative intestinal atony, and the authors therefore consider a 95 per cent success rate to be highly significant.

**3.** None of the patients receiving d-pantothenyl alcohol on a prophylactic basis, had any ill effects attributable to this medication. Even with an increase frequency of administration, there was no evidence of local or systemic toxicity; cardiovascular function and uterine muscle action were not adversely affected. It did not produce cramping or hyperperistalsis.

**4.** Because of its wide margin of safety, as well as its demonstrated effectiveness in minimizing the risk of postoperative ileus, we recommend d-pantothenyl alcohol be administered on a routine basis following intra-abdominal surgery.

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# Comments on Doctors' Business Problems

By Eugene P. Rister, C.P.A., *El Paso*

Perhaps one of the reasons Doctors study so long and work so hard is to accumulate enough money to speculate, have income tax problems, and have internal control problems.

## Income Tax

We want to touch briefly on some, not all, of the income tax changes passed by the Congress in September 1958, most of which do not affect you as practitioners, but may be of interest to you in your business ventures.

1. First the Pseudo Corporation—where small business corporations having no more than 10 stockholders may elect to pass the income directly to the stockholders. This provides the advantages of limited liability through corporate form, while avoiding the corporate income tax. This is not available if over 20 per cent of the gross income is from rents, interest and dividends. Of course, if you are already above the 50 per cent tax bracket, you may prefer to let the income be taxed to the corporation at the current corporate rates of 30 per cent on the first $25,000 of taxable income and 52 per cent above $25,000.

2. One of the changes by the 1958 technical amendments act was to increase the amount to $100,000 that can be accumulated as surplus before corporate dividends may be required.

3. An operating loss can now be carried back three years and then forward for five years.

4. A point that will be applicable to all of you is the new "additional depreciation" provision. For personal property acquired after December 31, 1957, having a useful life of at least six years, an immediate write-off of 20 per cent of the cost will be allowed in addition to the regular depreciation, to the extent of property having a cost of $10,000 (or $20,000 on a joint return). Note that this is personal property, and not real estate.

5. Leasehold improvements and lease cost—will now have to be amortized over the life of the lease, including any option periods, unless certain requirements are met.

6. Effective Jan. 1, 1959 the social security rates were increased so that you should now be deducting 2½ per cent social security from your employees salaries.

## Investments

If you have an adequate income you have probably been considering investments. Strictly from income tax considerations, you are probably aware of the $50 exclusion (or $100 on a joint return) of dividend income received from domestic corporations, and the 4 per cent credit against the tax for dividends that are included in the return. Therefore, you should have at least $100 of dividend income. This does not include interest from Federal Savings & Loan Associations, or any tax free organization—such as cooperatives, or dividends on insurance policies. If you do not have time to study the stock market, mutual funds have provided a good way to invest regularly in a stock market that always comes back higher, and at the same time gives you both some dividend income and capital gain income. You are reminded that you must pay tax on the dividends even though they are reinvested for you.

You may want to consider municipal or State Bonds—for their tax free return. A $1,000 investment yielding 6 per cent to a Doctor in the 60 per cent tax bracket is actually a yield of only 2.4 per cent after income taxes. While you cannot deduct interest borrowed to carry taxfree bonds, there is a possibility of making a good return by borrowing most of the cost of the bonds, at a low interest rate charged on loans secured by such securities. A tax free return on the money invested of as high as 10 to 15 per cent can sometimes be made. Ask your banker or broker about this class of investment.

## Oil

Nearly every Doctor has at some time been introduced to the tax advantages of investments in oil. Not only is there usually a complete charge off, but if a producing well is drilled, all of the intangible drilling costs can be charged off, and there is the 27½ per cent depletion allowance on income from oil produced. You probably should be in the 60 per cent tax bracket before going into good oil ventures. For a married taxpayer having

$32,000 of taxable income (after all deductions), the tax bracket is 50 per cent and 60 per cent at $44,000.

Another field of investments that you may be interested in is real estate, where an income tax deduction will be allowed for depreciation of buildings, although the property may be increasing in value.

### Internal Control

You may have income tax problems, and investment problems, even though you do not have a good system of internal control, but it is not fair to your employees, or to your practice if you tempt employees by your accounting methods. You should not have any employee that you do not have implicit faith in, and even then you should use every safeguard.

What safe-guards should we consider?

1. First—check the references and employment records of new aides. Watch for any skips in employment, and confirm dates of employment with previous employers.

2. Even though you are sure they can be trusted, bond them. It is considered good, standard business practice. Unless you follow other safeguards, increase the bond. Insist on annual vacations for all employees.

3. Divide the duties if at all possible. (a) Separate the receiving of cash from the postings to the individual accounts. (b) Have someone other than the bookkeeper open the mail. It is good for the doctor to do it if possible.

4. You should have an adequate system of making certain that all billings are properly recorded, both in the daily log and on the customers accounts. Posting to the accounts should be carefully cross-referenced, and dated.

5. Use numbered receipts. Require copy of receipt be given for all cash payments.

6. Deposit all cash received. It may be the only way you can later prove the amount of an embezzlement (by a comparison of receipts with amounts deposited).

7. Make all deposit slips in duplicate.

8. Periodically review the system, and make checks yourself. Check the patient's statements against the account ledger sheets, and have someone other than the bookkeeper mail them. Have the accounts confirmed once a year by an independent auditor.

9. Certainly keep a General Ledger, and an Accounts Receivable Control, against which the detail of the accounts should be balanced at least monthly.

10. Periodically test the additions of columns. Request your auditor to do this as part of his audit procedures.

11. Doctor should receive the bank statement directly from the bank, and should at least periodically reconcile the bank balance.

12. Pay all expenses by check, even petty cash disbursements.

13. Machine accounting provides many good internal control features not otherwise available, and usually reduces the time requirement for bookkeeping. The investment in a machine that provides control totals on receipts and accounts receivable charges will be a very small percentage of your cash movement over a ten year period.

14. You should have an annual audit by a Certified Public Accountant, and you should have him review your accounting sytem and controls periodically.

# MONTHLY CLINICAL PATHOLOGICAL CONFERENCE
# EL PASO GENERAL HOSPITAL

June 18, 1959

FREDERICK P. BORNSTEIN, M. D. — *Editor* — *Case No. 1254*

Presentation of case by Walter D. Feinberg, M. D.

**History:—Dr. Nathan Kleban:**

A 64-year-old divorced, unemployed man of Negro and Latin-American parentage was brought to the hospital by ambulance.

For many years the patient had been a heavy alcohol drinker. In 1956 a chest film was negative for heart or lung disease. The patient had subsisted almost entirely on wine for about two months before admission. He complained of poor appetite and inability to walk. His skin color was said to have undergone no change at any time. No other history was recorded.

**Physical Examination:**

The patient was able to sign his name legibly on admission, although he was confused when he reached the ward. Mucous membranes were deeply jaundiced. Skin was fairly heavily pigmented with icteric gray tint. Rectal temperature was 96.4; pulse 100; respirations 24; blood pressure 112/50. There were ecchymoses on both forearms. Arcus senilis was present bilaterally. Teeth were carious. Tonsils were enlarged and pharynx was mildly injected. Arteriolar nevi were present on the upper trunk. There were frequent premature cardiac systoles. The abdomen was protruberant but soft. Liver edge extended four cm. below the right costal margin. Pubic hair was scanty. There was an equivocal extensor plantar reflex.

**Hospital Course:**

During the seven weeks he was in the hospital the patient was free of fever except for the first and last week. Confusion and restlessness were followed by coma. With intensive therapy he began to improve, was able to sit in a wheel chair, to walk with assistance, and to take a high protein, high carbohydrate, low fat diet. Medications included whole blood transfusions, prednisone, multivitamins, chlorothiazide, aminophylline, vitamin K, methionine, and antibiotics.

Lethargy, somnolence, stupor and coma recurred. There were repeated convulsions for several hours prior to death.

**Laboratory Findings:**

**Blood counts: 2-22-59**—Hb. 5.3 gm.%, WBC 9,650, Stabs. 5, Segs. 69, Lymphs 26; **2-24-59** — Hb. 7.0 gms.%, Ht. 23 vol.%; **2-26-59 —** Hb. 9.9 gms.%, RBC 2,820,000, WBC 12,800 (reticulocytes 3.7%), Stabs. 9, Segs. 73, Lymphs. 14, Monos. 3; **3-8-59 —** Hb. 10.7 gms.%, Ht. 31%; **3-12-g9** — Hb. 11.9 gm.%, Ht. 35%, **3-19-59** — Hb. 12.4 gm.%, Ht. 41 vol.%, WBC 13,100, Segs. 70, Lymphs. 27, Eosins. 2, Monos. 1.

**Urinalyses: 2-22-59** — Amber, hazy, alkaline, S.G. QNS, albumin 4+, sugar neg., WBC 20-30/hpf, innumerable RBC, few sq. ep. cells; **2-23-59**—Amber, turbid, acid, S.G. 1.017, albumin 2+, sugar neg., bile neg., urobilinogen neg., innumerable RBC; **3-30-59 —** Bile negative, urobilinogen 1:80 (normal 1:20).

**Chemistry: 2-21-59** — Van der Bergh Direct—0.655, Indirect—2.02; **2-22-59**—Urea Nitrogen 28.2gm.%, **2-23-59** — $CO_2$ capacity—25 mEq/L, Cholesterol total—75 mg.%, Cholesterol esters — (75-150) 10 mg.%, Chlorides (as NaCl) — 105 mEq/L, Glucose—303 mg.%, Phosphatase, Alk. —4.9, Urea Nitrogen—26.0 mg.%, Potassium — 5.3, Sodium 135; **2-25-59**—Glucose—170 mg.%, Van den Bergh Direct — 2.00, Indirect — 4.22; **2-27-59**—Total protein—7.5 gm.%, Albumin—4.1, Globulin—3.3, A/G—1.2/1, Van den Bergh Direct —4.0, Indirect — 4.4, Ketosteroids — .72 mg.%; **3-2-59**—Total protein—8.8 gm.%, Albumin—5.5 gm.%, Globulin—3.5, A/G—1.67; **3-6-59** — Van den Bergh Direct—.770, Indirect—2.31; **3-19-59** — Glucose — 125 mg.%, Urea Nitrogen — 20.8;

**3-28-59**—Glucose—195 mg.%, Urea nitrogen—30.7.

**Thymol turbidity: 2-23-59**—9 units; **2-27-59**—12.7; **3-21-59**—1.5; **4-1-59**—2.0 units.

**Cephalin flocculation: 2-24-59**—24 hours 4+, 48 hours 4+; **3-21-59**—24 hours 1+, 48 hours 2+; **4-1-59**—24 hours 3+, 48 hours 4+.
**Coagulation time—2-24-59** — 6 seconds, bleeding time 3 minutes.

**Bence Jones Alb.—2-24-59**—Negative.

**PBI and free iodine: 3-2-59**—3.4 (3.1 free); **3-6-59**—2.6 (2.6 free).

**RBC fragility: 3-6-59**—Partial hemolysis at 40%, Complete hemolysis at 30%, Control partial—42%, Control complete—34%.

**Serum iron—3-12-59**—0.18 mg.% (normal .05-.25 mg.%).

**Serology—2-25-59**—Negative.

**Stool exam.: 3-25-59**—Occult blood and gross positive — bile 4+ — urobilinogen negative — few endamoeba coli cysts seen.

**Stool culture**—Negative.

**Sputum—2-22-59**—Smears and cultures negative for acid-fast.

**Prothrombin time—3-24-59**—90%.

**Glucose tolerance: 3-3-59**—Fasting 195 mg.%, ½ hr. 235 mg.%, 1 hr. 313 mg.% (patient had a portion of his breakfast), 2 hr. 303 mg.%, 3 hr. 322 mg.%, 4 hr. 332 mg.%; **3-10-59**—Fasting—165 mg.%, ½ hr. 210 mg.%, 1 hr. 250 mg.%, 2 hr. 303 mg.%, 3 hr. 322 mg.%, 4 hr. 332 mg.%.

**X-Rays: 2-21-59—Conclusions:** Abdomen negative for evidence of mechanical obstruction; **2-25-59**—Re-examination of the chest and comparison with previous study reveals no significant change from the previous examination; **3-5-59**—Re-examination of the chest reveals no change since the previous examination. There is no evidence of acute process or congestive failure. The upper abdomen is dense and there is bulging of the flank consistent with an ascites. **3-11-59.** Conclusion: Negative for evidence of ulcer or neoplasm. **3-24-59**—Chest and abdomen—Conclusion: Negative for evidence of biliary calculus. **3-27-59**—Survey film of the abdomen reveals no evidence of intestinal obstruction. There is a moderate amount of small bowel gas consistent with an adynamic ileus. There is no evidence of peritonitis, free fluid or soft tissue masses. There is considerable calcification of the abdominal and pelvis blood vessels with no evidence of a calculus opaque to X-ray overlying either urinary tract or gall bladder area.

**Electroencephalogram:**—"This record shows a diffuse generalized toxic type of reaction with very low voltage and consistent with the clinical diagnosis of hepatic coma. There is no localization or focal activity or primary disease of brain. There is no paroxysmal activity of the convulsive disorders. Abnormal electroencephalograms: toxic type of record with coma clearing to a semi-conscious level and fading again to coma" (no date given).

**Electrocardiogram—2-22-59** — Diffuse mild subepicardial ischemia.

**Clinical Discussion: Dr. Walter Feinberg:**

When I first looked over this history it looked like a very straightforward case of alcoholic cirrhosis, but my suspicions of Dr. Bornstein had already been aroused by other people so I read it a second time. This patient had a history of heavy alcoholism, apparently came in in liver coma and got out of liver coma and relapsed, not to come out of it that time. I would like to ask one or two questions if I may about the protocol, and that is with regard to the urinalysis on February 22 in which innumerable red cells were seen. Was this due to an indwelling catheter? Can anyone tell me? This man was supposed to be disoriented. I presume that he had a catheter in to account for that, is that right?

**Dr. Soloff:**

Yes.

**Dr. Feinberg:**

There are several features of the laboratory work that are a bit unusual. The first thing that bothered me a little bit was the extreme anemia on admission. The anemia is certainly more than is commonly seen in ordinary alcoholic cirrhosis without a history of bleeding. The serum bilirubin initially showed mostly indirect reacting bilirubin and later a considerable portion direct. This also is surprising for pure alcoholic cirrhosis.

Another thing that was a little bit surprising was the globulin and albumin of 4.1 grams percent with a relatively normal globulin. I would like to take this opportunity to comment on the serum bilirubin. I think it is probably now a matter of general knowledge, but we used to think of the

bilirubin as bilirubin globin and
.ng bilirubin as bilirubin itself.
s have now been identified and
it is now known that the indirect reacting substance is bilirubin itself and that what the liver does is to conjugate bilirubin with a glucoronide which makes it a water-soluble product, and the direct reacting substance is actually a bilirubin gluconide. I think Watson's theories are still of value, but at least the concept of bilirubinglobin has been changed.

Now the differential diagnosis in this case rests in thinking of the diseases that might cause severe cirrhosis and diabetes combined. So one begins to think of whatever disease might be present other than or in addition to an alcoholic cirrhosis. I might comment again for a minute about the low hemoglobin, simply to say that it has been shown with isotopes that patients with cirrhosis of the liver actually do not have hemolytic anemia. Actually they lose more blood in the stool than is recognized, 50 to 200 cc. of blood daily, without obvious bleeding, without known varices, without known bleeding lesions and without having melena; so a patient with cirrhosis may be severely anemic from gastro-intestinal bleeding without an obvious bleeding source.

### Pancreas and Liver

Then we have to think of conditions that involve the pancreas and the liver combined. Obviously from the interest that was shown with the abdominal films, the house staff was thinking in terms of something acute in the abdomen. I wondered about an acute pancreatitis, or an acute hemorrhagic pancreatitis in a patient with alcoholic cirrhosis. This would not be an uncommon situation but the fact that he came out of it would influence me against the diagnosis of an acute pancreatitis. Carcinoma of the pancreas is also a possibility in a man with cirrhosis. He might develop diabetes. I simply cannot exclude this possibility on the basis of the information that I have here. He might have alcoholic cirrhosis and a chronic pancreatitis. However, pancreatitis is characterized by episodes of pain and pancreatic calcification. There is no comment about this on the abdominal film, so that seems less likely.

The house staff obviously were scratching their heads pretty much because they got PBI's and things like that, some ketosteroids, but I doubt that these were really too helpful. There were a few amoeba cysts seen, and hepatic abscess is a possibility, but again it seems less likely in this particular situation.

Wilson's disease is a situation in which one finds evidence of cirrhosis, convulsions, or ataxia and glycosuria as well as aminoaciduria. The main feature in this history right from the very beginning that would tend to rule out Wilson's disease is the age of the patient—they usually don't get this old. This patient was 64 years old.

The other condition one thinks of as causing diabetes and cirrhosis of the liver is hemochromatosis. The house staff was obviously thinking of that. There are some items in the protocol that suggest this diagnosis. I didn't quite understand why in a three paragraph protocol there was so much comment about the color of the skin. However, in the presence of a normal serum iron I think that the diagnosis of hemochromatosis is only to be suspected and that in a patient who already has a pigmented skin, the diagnosis probably can be made only by the pathologist.

In summary, then, I think this was cirrhosis of the liver, cause uncertain, possibly alcoholic. I cannot exclude hemochromatosis as a strong possibility. I think that cancer of the pancreas is less likely. I would like to comment about the demise of this patient. The patient came into the hospital in hepatic coma, and then was brought out of hepatic coma. Then he was given a high protein diet and chlorothiazide. Now both high protein diet and chlorothiazide are known to precipitate hepatic coma and it may be that the terminal episode was unfortunately precipitated by the medical management, and I think he died in a hepatic coma.

**Dr. Postlewaite:**

I am interested in the comment that there was hepatic coma. The patient had every reason for coma. The renal situation is abnormal—albumin, blood, other elements here, urine nitrogen retention, there is a possibility of renal disease. He's a diabetic, so he could be pancreatic with diabetic coma, although the $CO_2$ power is remarkably normal for a person in diabetic coma. He is apparently confused off and on, and he's got a good reason to have cerebral coma. Perhaps there is a vascular problem, I haven't seen anything about sickle cell, and I don't even recall the serology anywhere in here. Then finally we have anemia, which may produce coma on an anemic basis,

but that seems untenable. Now back to liver disease. Here is a serum iron which is not against hemochromatosis. We had that experience already; with a hemochromatosis the serum iron is normal. Apparently the liver biopsy or skin biopsy are the only way to obtain a conclusion. In a man with a black skin it would be somewhat difficult to recognize hemochromatosis, although he has a very typical situation, large liver—I don't see the spleen enlarged; is that commented on?

**X-Ray Discussion—Dr. Vincent Ravel:**

In the chest pictures of 1956 and March of 1959 we could demonstrate nothing really significant. As far as an hepatic abscess is concerned that right hemidiaphragm looks real well and there is no pleural effusion, or compression phenomena that you usually get with liver abscesses. I don't see any pancreatic calcifications. He never had any signs of mechanical obstruction. The aorta is markedly calcified and the gastric mucosa looked perfectly all right. There is no evidence of widening of the duodenal loop.

**Dr. Postlewaite:**

Well, additional findings were those of circulatory problems, not only anemia but also myocardial damage and there is another possible cause for coma. Now back to the liver which is apparently what we ought to stay with. Hepatic coma in the face of hyperglycemia I think is a little unusual. One would wonder then what the pathology in the liver was and the one that fools us worst is the carcinoma of the liver which can't be diagnosed, even by the surgical groups, for some reason or other, and we lose them rather regularly and it's an autopsy diagnosis apparently.

**Dr. Solomon Heller:**

Very low cholesterols may be seen with very severe anemias of any type and therefore the cholesterol could be well way out of proportion to liver damage. Incidentally, the anemia on admission seemed to be an iron deficiency type which could be due to intestinal bleeding. Interestingly enough, the serum iron, 180 micrograms, is elevated and if you want to get anything out of serum irons you should do an iron-binding capacity. If you don't do that, you don't really know what the iron means.

**Dr. Saul B. Appel:**

The protocol doesn't tell us the amount of chlorothiazide that was used, but assuming that the patient had ascites I imagine the diuretic diuril or chlorothiazide was being used to attempt to reduce his edema and ascites. This medication is particularly liable to give you trouble in a patient with cirrhosis of the liver, where you can very easily produce hypokalemia. There is a very interesting study that Dr. Stern did many years ago in New York, in which he described the stupor and coma and other cerebral manifestations in patients who dehydrated and had electrolyte imbalances. Possibly the cerebral syndrome toward the end of this patient's course might have had something to do with an electrolyte imbalance.

**Dr. William Gaddis:**

I would like to say that we presented this patient at Saturday morning conference here. There was quite some spirited discussion. Two or three of the doctors visited the patient on the ward and when the discussion was ended we didn't have any more idea than those of you who are sitting here tonight what his real trouble was. It was quite obvious that we were not aware of all the factors that were present in this patient's illness to be able to come up with a proper antemortem diagnosis, and I feel like we are probably going to be somewhat surprised when Dr. Bornstein lowers the boom on us.

**Clinical Diagnosis:** Jaundice, cause unknown—arteriosclerotic cardiovascular disease.

**Dr. Feinberg's Diagnosis:** Cirrhosis of the liver, possibly alcoholic; Hemochromatosis as a strong possibility.

**Pathological Diagnosis:** 1. Hemochromatosis, especially of the liver, pancreas and heart; 2. Cirrhosis of liver, hemochromatosis type; 3. Confluent bronchopneumonia, right upper lobe.

**Pathological Discussion — Dr. Frederick P. Bornstein:**

Before I started the autopsy Dr. Soloff threw the case at me and I suggested hemochromatosis and he said, "Ha ha, the patient is half Indian, half Negro, and the color of the skin never changed." I have always learned that the history is the most important part of the diagnosis, but some of these cases make you wonder about that.

He had a rather unusually dusky color. The visceral as well as the parietal peritoneum had the same dull gray discoloration which was noted in the skin. The liver was rather small. There was obvious bronchopneumonia which probably rep-

resented the terminal event. The liver was rather small but in spite of the smallness weighed 1500 grams. The surface of the liver was dark brown and finely lobulated. The lobulation was somewhat irregular, not the type found in Laennec's cirrhosis. The lobulation was caused by bands of connective tissue much thicker than in common cirrhosis, so that a superficial nodular pattern of large, irregular nodules was produced. On sectioning, the liver pattern had gone and again one saw large, irregular, deep brown liver lobules. The pancreas had the same dark brown discoloration. The small intestine had a mucosa which was coal black and a preliminary gross diagnosis of hemochromatosis with cirrhosis of the liver and changes in the pancreas, was made.

On microscopic examination the liver stained with Prussian blue reaction for hemosiderin showed a classical pattern of hemochromatosis. Every individual liver cell contained hemosiderin granules. In the pancreas the islands of Langerhans contained large amounts of hemosiderin. Even in an unstained lymph node, golden brown pigment was quite obvious, demonstrating the large extent of the process. The real relation between hemochromatosis and cirrhosis of the liver and the intermediary metabolic processes are certainly not clearly understood. The disease has one peculiarity, more carcinomas of the liver arise from hemochromatotic livers than even cirrhotic livers. With this goes another peculiarity for which I have no explanation. Old liver tissue is hemochromatotic. If there are tumor islands of regenerating liver tissue one sees cells which imitate hepatic cells but which do not accept the hemosiderin.

Concerning the skin in this particular case, it is usually and generally accepted that the skin is involved in the process. However, a number of skin sections failed to reveal any hemosiderin in the skin, so I cannot tell you whether or not the skin was involved in this case. I have no evidence that it was. The heart, liver, pancreas, lymph nodes and all the endothelial surfaces were definitely involved.

**A Physician**

The literature implies that the deaths of hemochromatotics are cardiac failures.

**Dr. Bornstein:**

Well, this particular case died from bronchopneumonia. The spleen was small, by the way.

**Dr. Heller:**

There is a great deal of controversy in this field as to what constitutes a primary hemochromatosis, a secondary hemochromatosis or hemosiderosis. Basically hemochromatosis is supposed to be an abnormality in the absorption of iron. These people actually absorb iron out of proportion to their needs and hemosiderosis has been found in people who have received as little as one transfusion. Very often these hemosiderotics also suffer from aplastic and hemolytic anemias, diseases with which they have multiple transfusions. However, there are a number of reports where hemosiderosis has appeared after only two or three transfusions.

There is a triad in this hemochromatosis that is heart, diabetes and testicular atrophy along with cirrhosis. As far as the diagnosis is concerned this is one place where your serum iron is of considerable importance. If in this case (180 micrograms percent) we had had an iron binding globulin, there would probably have been 100 percent saturation, which in itself would have given you the diagnosis. Normally, there is a third, or 33 percent saturation.

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